Amendments to the Specification:

Insert the paper copy of the Sequence Listing filed herewith following the Drawings.

Please replace paragraph [0016] on page five with the following paragraph:

[0016] Unless otherwise noted, "BACE" is Beta-site APP Cleaving Enzyme, and is the β-secretase enzyme that cleaves β-amyloid precursor protein (APP) at residue 671 (770aa isoform of APP numbering). After cleavage of APP by BACE, the remaining APP is cleaved at residue 716 by γ-secretase, leaving a 42 amino acid fragment of APP that is found in the proteinaceous plaques of Alzheimer's patients. The amino acid sequence of BACE preferably has the amino acid sequence deposited with Swiss Prot under accession number P56817 (SEQ ID NO:1), including conservative substitutions. As used herein, BACE also includes "BACE peptides," which are mlecules having less than the complete amino acid sequence of BACE. Preferaly, BACE peptides include the active site in which BACE binds to and cleaves APP. Most preferably, the BACE peptide corresponds to amino acid residues 58-447 set forth in Figure 1 ("$BACE_{58-447}$"), including conservative substitutions.

Please replace paragraph [0017] on page 5 with the following paragraph:

[0017] "APP" is β-amyloid precursor protein having the amino acid sequence deposited with Swiss Prot under accession number CAA31830 (SEQ ID NO:2), including conservative substitutions. As used herein, APP also includes "APP peptides," which are molecules having less than the complete amino acid sequence of APP. Preferably, APP peptides include the active site in which APP is cleaved by BACE.

Please replace the paragraph [0018] on page 6 with the following paragraph:

[0018] An "APP inhibitor peptide" is a peptide which inhibits binding between BACE and APP. Preferably, the APP peptide has the amino acid sequence SER-GLU-VAL-ASN-Sta-VAL-ALA-GLU-PHE (SEQ ID NO:3), where Sta is rare amino acid (S)-Statine.

Please replace paragraph [0028] on page 8 as with the following paragraph:

[0028] The present invention is directed to a crystallized complex of BACE and an APP inhibitor peptide that effectively diffracts X-rays for the determination of the structural coordinates of the complex. As used herein, BACE prefereably corresponds to $BACE_{58-447}$ as set forth in Figure 1, with the N-terminal domain consisting of amino acid residues 58-207 shown in Figure 1, and the C-terminal domain consisting of amino acid residues 208-447 shown in Figure 1. The APP inhibitor peptide is preferably SER-GLU-VAL-ASN-Sta-VAL-ALA-GLU-PHE (SEQ ID NO:3).

Please replace paragraph [0039] beginning at page 12 with the following paragraph:

[0039] Cloning of Human BACE1. Human polyA+ mRNA from whole brain (Clontech) was converted to cDNA by random-priming using Thermoscript RT-PCR System, according to the manufacturer's protocol (Lifetechnologies). This cDNA was amplified by PCR using the forward and reverse primers, 5' GCTCTAGAACCCAGC ACGGCATCCGGCTG 3' (SEQ ID NO:4) (XbaI site indicated by underlined sequence; nts. 517-537 in accession no. AF190725) and 5' CCAAGCATGCGGCCGCAATAGGCTATGGTCA TGAGGGTTGAC 3' (SEQ ID NO:5) (NotI site indicated by underlined sequence; nts. 1809-1833; bold "A" indicates additional nucleotide to permit in-frame translation of the Fc chimera; see below), respectively. PCR was accomplished using Expand Long Polymerase kit according to the manufacturer's conditions (Roche Biochemicals; buffer #3), with PCR cycling consisiting of an initial denaturin step at 95°C for 3min, 30-40 cycles of denaturation at 94°C for 30 sec, annealing at 65°C for 30 sec, elongation at 68°C for 1min 30sec, followed by a final elongation at 68°C for 5min. The PCR products were run on a 1% agarose gel. The appropriate band was cut out of the gel, purified by Quantum Prep Freeze'N Squeeze DNA Extraction Columns (Bio-Rad), and cloned into the SpeI/NotI sites of the mammalian expression vector, pED/Fc (Kaufman, RJ et al., 1991, Nucl. Acids. Res. 19:4485-4490).

Please replace paragraph [0042] beginning at page 14 with the following paragraph:

[0042] Purification of BACE1. For the purification of BACE the 102 liters of conditioned media was used. During purification the activity of the enzyme was estimated at room temperature by continuously monitoring the fluorescent intensity for 5-10 min. at 420 nm (ext - 320 nm) Abz-Ser-Glu-Val-Asn-Leu-Asp-Ala-Glu-Phe-Arg-Dpa (SEQ ID NO:6) (Abz=Amino benzoic acid, Dpa=9,10-diphenylanthracene) as the substrate. The reaction mixture contained 20 .mu.M of substrate, different amounts of enzyme in 0.5 ml of 20 mM Tris-HCl pH 8.0 and 100 mM NaCl. The concentrated material of conditioned media(1.6 1) was applied to column (2.8.times.12 cm) containing ImmunoPure Immobilized Protein A agarose (Pierce, Il., USA) equilibrated in PBS buffer. The speed of application was 2 ml/min. The column was washed with 1 liter of PBS buffer and the BACE-Fc protein was eluted by ImmunoPure IgG Elution Buffer (Pierce, Il., USA). The fractions containing protein were immediately neutralized by 1 M Tris-HCl to pH 8.0.

Please replace paragraph [0046] beginning at page 15 with the following paragraph:

[0046] Crystallization. The crystals were grown using the hanging drop vapour diffusion method. The protein was concentrated to mg/ml in 20 mM Tris pH 7.5, 200 mM sodium chloride. Inhibitor peptide sequence is SEVNStaVAEF (SEQ ID NO:3), where Sta is the rare amino acid (S)-Statine. It was concentrated to 100 mM in 100% DMSO and mixed with concentrated protein in a two-fold peptide excess to form the complex. 1 µl of complex was added to 1 µl of well solution containing 100 mM Sodium Cacodylate pH6.5, 25% PEG8K, 300 mM lithium sulphate. Plate-like crystal clusters grew within one week to dimensions of 200 µm times.400 µm times75 µm. Single crystals were transferred to a stabilizing, cryoprotectant solution which contained the well solution plus 25% Glycerol for a brief, 10 second, soak and then frozen in liquid nitrogen. X-ray diffraction crystals had space group 1222, and unit cell parameters a=86.627, b=130.861, c=130.729, and $\alpha=\beta=\gamma=90°$.